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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/658,659	09/08/2000	Vincent P. Stanton JR.		3340

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	28

DATE MAILED: 02/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/658,659	Stanton
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 20, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *182-201* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *182-201* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Continued Examination Under 37 CAR 1.114

1. A request for continued examination under 37 CAR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after allowance. Since this application is eligible for continued examination under 37 CAR 1.114, and the fee set forth in 37 CAR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CAR 1.114. Applicant's submission filed on November 20, 2002 has been entered.

Claim Rejections - 35 USC § 112

2. ***The following is a quotation of the second paragraph of 35 U.S.C. 112:***

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 182-201 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 182-191 are rejected because it is not clear if the intervening sequences between nucleotides 120 and 464 and 519 and 668 and 1059 and 1289 and 1308 and 1784 of SEQ ID NO: 1 are essential requirements or not for the claimed probes. For example, while 15 contiguous nucleotides are required, it is indefinite whether a probe in which nucleotides 105-120 of SEQ ID NO: 1, with the C of nucleotide 120, was extended one nucleotide to incorporate the G of 464

would fall within the scope of the claim. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 182, 188, 190, 192, 198, and 200 are rejected under 35 U.S.C. 102(b) as being anticipated by Rozen et al. (PCT International Publication Number: WO 95/33054) (December 7, 1995).

Rozen et al teach an isolated nucleic acid probe comprising at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1 (methylenetetrahydrofolate reductase), the probe comprising nucleotide 120 wherein T is replaced by C (Abstract and Figure 1A).

Rozen et al teach the probe comprising DNA and a detectable label (Abstract, Page 34, lines 23-25, and Claim 1 and Figure 1A and Page 18, lines 18-35).

Rozen et al teach a method comprising:

a) providing a sample comprising nucleic acid molecules present in a biological sample obtained from a patient (page 21, line 13 to page 23, line 28);

b) contacting the sample with a probe comprising at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO: 1 (methylenetetrahydrofolate reductase), the probe

comprising nucleotide 120 wherein T is replaced by C (Abstract and Figure 1A and claim 2 and page 21, line 14 to page 22, line 25); and

c) determining if the sample comprises a nucleic acid molecule that hybridizes to the probe (page 21, line 14 to page 24, line 8).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 184-187, 191, 194-197 and 201 are rejected under 35 U.S.C. 103(a) over Rozen et al. (PCT International Publication Number: WO 95/33054) (December 7, 1995) in view of Haughland et al. (U.S.Patent 5,443,986) (August 22, 1995).

Rozen et al teach the probe and method of claims 182, 188, 190, 192, 198, and 200 as described above.

Rozen et al do not teach a shorter probe comprising no more than 50-500 contiguous nucleotides and fluorescent label.

Haughland et al teach a shorter probe comprising no more than 50-500 contiguous nucleotides and fluorescent label (Column 25, lines 21-47).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a shorter probe comprising no more than 50-

500 contiguous nucleotides and fluorescent label of Haughland et al. into the probe and method of Rozen et al, since Haughland et al. state, "Modern DNA synthesis has permitted an automatic and routine preparation and labeling of an oligonucleotide with lengths up to about 100 bases. (Column 25, lines 32-34)." Haughland et al further provide motivation as Haughland et al. state, "The substrates in this invention represent an important advance in situ hybridization for mRNAs, viruses as well as genomic DNA (Column 25, lines 45-47)". By employing scientific reasoning, an ordinary artisan would have combined and substituted a shorter probe comprising no more than 50-500 contiguous nucleotides and fluorescent label of Haughland et al. into the probe and method of Rozen et al, in order to improve the sequencing of nucleic acids of patients with methylenetetrahydrofolate reductase gene abnormality. An ordinary practitioner would have been motivated to combine and substitute a shorter probe comprising no more than 50-500 contiguous nucleotides and fluorescent label of Haughland et al. into the probe and method of Rozen et al, in order to achieve the express advantages noted by Haughland et al., of an invention that represents an important advance in situ hybridization for mRNAs, viruses as well as genomic DNA.

8. Claims 189 and 199 are rejected under 35 U.S.C. 103(a) over Rozen et al. (PCT International Publication Number: WO 95/33054) (December 7, 1995) in view of Cohen et al. (U.S.Patent 6,232,456 B1) (May 15, 2001).

Rozen et al teach the probe and method of claims 182, 188, 190, 192, 198, and 200 as described above.

Rozen et al do not teach a probe comprising a peptide nucleic acid.

Cohen et al teach a probe comprising a peptide nucleic acid (Column 13, lines 41-63).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a probe comprising a peptide nucleic acid of Cohen et al. into the probe and method of Rozen et al, since Cohen et al. state, "PNAs are naturally charged moieties which can be directed against RNA targets or DNA. PNA probes used in assays in place of , for example, the DNA probes of the present invention, offer advantages not achievable when DNA probes are used. These advantages include manufacturability, large scale labeling, reproducibility, stability, insensitivity to changes in ionic strength and resistance to enzymatic degradation which is present in methods utilizing DNA or RNA (Column 13, lines 47-55)." By employing scientific reasoning, an ordinary artisan would have combined and substituted a probe comprising a peptide nucleic acid of Cohen et al. into the probe and method of Rozen et al in order to improve the sequencing of nucleic acids of patients with methylenetetrahydrofolate reductase gene abnormality. An ordinary practitioner would have been motivated to combine and substitute a probe comprising a peptide nucleic acid of Cohen et al. into the probe and method of Rozen et al, in order to achieve the express advantages noted by Cohen et al., of PNA probes which offer advantages not achievable when DNA probes are used, which includes manufacturability, large scale labeling, reproducibility, stability, insensitivity to changes in ionic strength and resistance to enzymatic degradation which is present in methods utilizing DNA or RNA.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessauat reached at (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

January 22, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER